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Amino Acid Sequence Disclosures. Attached in compliance with this requirement is a paper copy and a computer readable copy of the Sequence Listing and a statement that the content of the paper and computer readable copies are the same, and, where applicable, include no new matter, as required by the appropriate subsections of 37 CFR 1.821.

III. Claim Objections

Claim 102 has been amended to rewrite the claim into proper multiple dependent format. In view of the amendment to claim 102, claim 103 is now also in proper format. As required by 37 C.F.R. § 1.121(c), the amended claim is rewritten with all changes included. With this amendment, the Examiner is requested to withdraw this objection.

IV. The Rejection Under 35 U.S.C. § 112, First Paragraph, Written Description

Applicants respectfully traverse the rejection of claims 1-28 and 102-103 under 35 U.S.C. § 112, first paragraph, for allegedly not complying with the written description requirement.

The Office Action states that the four examples of the methods for the modulation of a gene in a fungus to improve the production of a secondary metabolite is not deemed to be descriptive of a complete structure of a representative number of species encompassed by the claims. Applicants disagree and state positively that the specification does describe and identify how to modulate genes in addition to those actually shown in the specification and in fungal strains in addition to those actually demonstrated in the Examples. Further, the specification also provides a written description for identifying fungal homologs of the genes on page 22.

Applicants would point out that the claims currently pending in this application are directed to

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“a method for improving the production of a secondary metabolite by a fungus by increasing the yield of the secondary metabolite by modulating the expression of a gene involved in the regulation of a secondary metabolite production in a manner that improves the yield of the secondary metabolite” (claim 1);

“a method for improving production of a secondary metabolite by a fungus by increasing productivity of the secondary metabolite in the fungus by modulating the expression of a gene involved in the regulation of a secondary metabolite production in a manner that improves the productivity of the secondary metabolite” (claim 15);

“a genetically modified fungus” with the ability to produce secondary metabolites which was produced by any of the methods of claims 1-27 (claim 102); and,

“a method for making a secondary metabolite” by “culturing a genetically modified fungus according to claim 102 under conditions suitable for the production of secondary metabolites” (claim 103).

In the specification, beginning with the last paragraph on page 6 and continuing through page 31, a detailed disclosure is provided that teaches the characteristics of the claimed invention. In particular, specific genes listed on page 9 of the specification can be used to modulate the expression of a gene involved in regulation of a secondary metabolite by overexpression of the gene. Conditional expression of a gene is described on page 13, last full paragraph. Further, identifying a dominant mutation according to the invention is described in detail on pages 10 to 12, in numbered paragraphs 1 to 8. These dominant mutations can be dominant negative, dominant positive, or dominant neomorphic depending upon the phenotypic

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effect achieved by the mutation. Achieving the claimed invention through a peptide modulator activator or peptide modulator inhibitor is described in detail on page 12, last paragraph, through page 13, first two paragraphs. Modulation through mediation by a small molecule modulator is described on page 13, third full paragraph.

The Examples of the specification include actual working examples of the claimed invention.

In view of the details provided in the specification, Applicants aver that there is a representative number of species disclosed in the specification. In addition, one of skill in the art would recognize that Applicants were in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed and claimed. In conclusion, Applicants state that the disclosure meets the requirements of 35 U.S.C. § 112, first paragraph, as providing adequate written description for the invention as claimed. The Examiner is therefore requested to reconsider this rejection and to withdraw it.

V. The Rejection Under 35 U.S.C. § 112, First Paragraph, Enablement

Applicants respectfully traverse the rejection of claims 1-28 and 102-103 under 35 U.S.C. § 112, first paragraph, for allegedly not complying with the enablement requirement.

Applicants are submitting with this Response the Declaration of G. Todd Milne, Ph.D. Under 37 C.F.R § 1.132 which demonstrates the disclosure, as filed, enables the claimed invention for one skilled in the art at the time of filing.

Specifically, the Rule 132 Declaration provides Examples 1 to 7 using procedures described in the specification, with Figures 1 to 7, thus proving the enablement of the claimed

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invention by the specification. Example 1, demonstrating regulators of lovastatin production in *Aspergillus terreus*, provides further evidence that the specification supports claims 1, 2, 14-16, 28, 102 and 103. Example 2, showing regulators of penicillin production in *Penicillium chrysogenum*, provides further evidence that the specification supports claims 1, 2, 14-16, 28, 102 and 103. Example 3, exemplifying that the ganB G45R dominant active mutant variant increases lovastatin production in *Aspergillus terreus*, provides further evidence that the specification supports claims 1, 2, 4, 6, 14, 15, 16, 18, 21, 28, 102 and 103. Example 4, demonstrating that the gna3 G207A dominant negative mutant variant decreases lovastatin production in *Aspergillus terreus*, provides further evidence that the specification supports claims 1, 2, 4, 5, 14, 15, 16, 18, 19, 28, 102 and 103. Example 5, showing that the dominant neomorphic variant of An09 increases lovastatin production in *Aspergillus terreus*, provides further evidence that the specification supports claims 1, 2, 4, 7, 14, 15, 16, 18, 20, 28, 102 and 103. Example 6, illustrating that conditional expression of modulators increases lovastatin production in *Aspergillus terreus*, provides further evidence that the specification supports claims 1-4, 6, 14, 15, 16-18, 21, 28, 102 and 103. Example 7, illustrating small molecule modulators of secondary metabolite production, provides further evidence that the specification supports claims 1, 11-15, 25-28, 102 and 103.

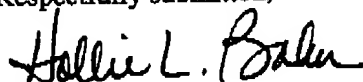
Applicants submit that the disclosure in the specification as further demonstrated by the evidence provided in the Rule 132 Declaration demonstrates that the claimed methods taught in the specification can be practiced by one of skill in the art without undue experimentation. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection.

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VI. Conclusion.

Applicants respectfully submit that all the bases for rejection of the pending claims are now moot. The Examiner is requested to reconsider the rejections and to withdraw them and to pass this case to issuance.

Respectfully submitted,



Hollie L. Baker
Registration No. 31,321

Date: *November 21, 2001*

Hale and Dorr LLP
60 State Street
Boston, MA 02109
Phone: (617) 526-6110
Facsimile: (617) 526-5000

Attachments: Compare copy of paragraph amended in specification
Compare copy of pending claim amended with this response

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COMPARE COPY OF
SPECIFICATION

This application claims priority under 35 U.S.C. § 119(e) to U.S. provisional application 60/160,587, filed October 20, 1999.

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COMPARE COPY OF
AMENDED CLAIM

102. A genetically modified fungus, wherein the genetically modified fungus has an ability to produce secondary metabolites and the ability of the genetically modified fungus to produce secondary metabolites has been improved by any of the methods of [claims 1-101] and claims 1-13 and 15-27.